SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Macrogol compound powder for oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains the following quantitative composition of active ingredients:

Macrogol 3350	13.125 g
Sodium Chloride	0.3507 g
Sodium Hydrogen Carbonate	0.1785 g
Potassium Chloride	0.0466 g

The content of electrolyte ions per sachet following reconstitution in 125 ml of water is equivalent to:

Sodium	65 mmol/l
Chloride	53 mmol/l
Hydrogen Carbonate (Bicarbonate)	17 mmol/l
Potassium	5 mmol/l

Excipients with known effect
Sorbitol (E420)
Sodium
Potassium

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution

Single-dose sachet containing a free flowing white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of chronic constipation.

4.2 Posology and method of administration

Posology

Chronic constipation
A course of treatment for chronic constipation with Macrogol compound powder for oral solution does not normally exceed 2 weeks, although this can be repeated if required. As for all laxatives, prolonged use is not usually recommended. Extended use may be necessary in the care of patients with severe chronic or resistant constipation, secondary to multiple sclerosis or Parkinson's Disease, or induced by regular constipating medication in particular opioids and antimuscarinics.

Adults, adolescents and the elderly: 1-3 sachets daily in divided doses, according to individual response.

For extended use, the dose can be adjusted down to 1 or 2 sachets daily.

Children below 12 years old: Not recommended.

Patients with renal insufficiency: No dosage change is

necessary. Method of administration

The oral solution is for oral use. Each sachet should be dissolved in 125 ml water.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, ileus, severe inflammatory conditions of the intestinal tract, such as Crohn's disease and ulcerative colitis and toxic megacolon.

4.4 Special warnings and precautions for use

The fluid content of Macrogol compound powder for oral solution when re-constituted with water does not replace regular fluid intake and adequate fluid intake must be maintained.

Diagnosis of impaction/faecal loading of the rectum should be confirmed by physical or radiological examination of the abdomen and rectum.

Mild adverse drug reactions are possible as indicated in Section 4.8. If patients develop any symptoms indicating shifts of fluids/electrolytes (e.g. oedema, shortness of breath, increasing fatigue, dehydration, cardiac failure) Macrogol compound powder for oral solution should be stopped immediately and electrolytes measured, and any abnormality should be treated appropriately.

The absorption of other medicinal products could transiently be reduced due to an increase in gastro-intestinal transit rate induced by Macrogol compound powder for oral solution (see section 4.5).

Seizure

Cases of seizures associated with use of macrogol 3350 with electrolytes for bowel preparation were observed in patients either with or without prior history of seizures. These cases were mostly associated with electrolyte abnormalities such as severe hyponatraemia (see section 4.8). Use caution when prescribing macrogol 3350 with electrolytes in patients with a history of seizures, at increased risk of seizure or at risk of electrolyte disturbance. In case of neurologic symptoms, fluid and electrolyte abnormalities should be corrected.

Oesophageal Rupture

Cases of oesophageal rupture (Boerhaave syndrome) associated with excessive vomiting after intake (see section 4.8) of macrogol 3350 with electrolytes for bowel preparation has been reported post-marketing, mostly in elderly patients. Advise patients to stop administration and seek immediate medical assistance if they experience incoercible vomiting and subsequent chest, neck, and abdominal pain, dysphagia, hematemesis or dyspnoea.

Ischaemic colitis

Post-marketing cases of ischaemic colitis, including serious, have been reported in patients treated with macrogol for bowel preparation. Macrogol should be used with caution in patients with known risk factors for ischaemic colitis or in case of concomitant use of stimulant laxatives (such as bisacodyl or sodium picosulfate). Patients presenting with sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis should be evaluated promptly.

Avoid mixing PEG laxatives and starch-based thickeners in patients with dysphagia, considered at risk of aspiration

This medicine contains potassium, less than 1 mmol (39 mg) per sachet, i.e. essentially 'potassium-free'.

This medicine contains 187 mg sodium per sachet, equivalent to 9% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

The maximum daily dose of this product is equivalent to 28% of the WHO recommended maximum daily intake for sodium.

Macrogol compound powder for oral solution is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

This medicine contains up to 50 mg sorbitol in each sachet. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

In patients with swallowing problems, who need the addition of a thickener to solutions to enhance an appropriate intake, interactions should be considered, see section 4.5.

4.5 Interaction with other medicinal products and other forms of interaction

Macrogol raises the solubility of medicinal products that are soluble in alcohol and relatively insoluble in water.

There is a possibility that the absorption of other medicinal products could be transiently reduced during use with Macrogol compound powder for oral solution (see section 4.4).

There have been isolated reports of decreased efficacy with some concomitantly administered medicinal products, e.g. anti-epileptics. Therefore, other medicines should not be taken orally for one hour before, during and for one hour after taking Macrogol compound powder for oral solution.

Macrogol compound powder for oral solution may result in a potential interactive effect when used with starch-based food thickeners. The polyethylene glycol (PEG) ingredient counteracts the thickening effect of starch, effectively liquefying preparations that need to remain thick for people with swallowing problems.

4.6 Fertility, Pregnancy and lactation

Pregnancy

There are limited amount of data from the use of Macrogol compound powder for oral solution in pregnant women. Studies in animals have shown indirect reproductive toxicity (see section 5.3). Clinically, no effects during pregnancy are anticipated, since systemic exposure to macrogol 3350 is negligible.

Macrogol compound powder for oral solution can be used during pregnancy.

Breastfeeding

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to macrogol 3350 is negligible.

Macrogol compound powder for oral solution can be used during breast-feeding.

Fertility

There are no data on the effects of Macrogol compound powder for oral solution on fertility in humans. There were no effects on fertility in studies in male and female rats (see section 5.3).

4.7 Effects on ability to drive and use machines

Macrogol compound powder for oral solution has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Reactions related to the gastrointestinal tract occur most commonly.

These reactions may occur as a consequence of expansion of the contents of the gastrointestinal tract, and an increase in motility due to the pharmacologic effects of Macrogol compound powder for oral solution. Mild diarrhoea, usually responds to dose reduction.

The frequency of the adverse effects is not known as it cannot be estimated from the available data.

System Organ Class	**Adverse Event**

Immune system disorders	Allergic reactions, including anaphylaxis, angioedema, dyspnoea, rash, urticaria, and pruritus.
Skin and subcutaneous tissue disorders	Erythema.
Metabolism and nutrition disorders	Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia.
Nervous system disorders	Headache, seizure.
Gastrointestinal Disorders	Abdominal pain, diarrhoea, vomiting, nausea, dyspepsia, abdominal distension, borborygmi, flatulence and anorectal discomfort, oesophageal rupture (Boerhaave syndrome).
General disorders and administration site conditions	Peripheral oedema.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Severe abdominal pain or distension can be treated by nasogastric aspiration. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxatives. ATC code: A06A D65

Macrogol 3350 acts by virtue of its osmotic action in the gut, which induces a laxative effect. Macrogol 3350 increases the stool volume, which triggers colon motility via neuromuscular pathways. The physiological consequence is an improved propulsive colonic transportation of the softened stools and a facilitation of the defaecation. Electrolytes combined with macrogol 3350 are exchanged across the intestinal barrier (mucosa) with serum electrolytes and

excreted in faecal water without net gain or loss of sodium, potassium and water.

Clinical studies in the use of macrogol 3350 in chronic constipation have shown that the dose needed to produce normally formed stools tends to decrease over time. Many patients, respond to between one and two sachets a day, but this dose should be adjusted depending on individual response.

5.2 Pharmacokinetic properties

Macrogol 3350 is unchanged along the gut. It is virtually unabsorbed from the gastro-intestinal tract and is excreted, unaltered, in faeces. Any macrogol 3350 that is absorbed is excreted via the urine.

5.3 Preclinical safety data

Preclinical studies provide evidence that macrogol 3350 has no significant systemic toxicity potential, based on conventional studies of pharmacology, repeated dose toxicity and genotoxicity.

There were no direct embryotoxic or teratogenic effects in rats even at maternally toxic levels that are a multiple of 66 x the maximum recommended dose in humans for chronic constipation. Indirect embryofetal effects, including reduction in fetal and placental weights, reduced fetal viability, increased limb and paw hyperflexion and abortions, were noted in the rabbit at a maternally toxic dose that was 3.3 x the maximum recommended dose in humans for treatment of chronic constipation. Rabbits are a sensitive animal test species to the effects of GI-acting substances and the studies were conducted under exaggerated conditions with high dose volumes administered, which are not clinically relevant. The findings may have been a consequence of an indirect effect of macrogol related to poor maternal condition as the result of an exaggerated pharmacodynamic response in the rabbit. There was no indication of a teratogenic effect.

There are long-term animal toxicity or carcinogenicity studies involving macrogol
3350. Results from these and other toxicity studies using high levels of orally administered high molecular weight macrogols provide evidence of safety at the recommended therapeutic dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica

Saccharin sodium

Orange flavour (Orange flavour contains: flavouring substances and flavouring preparations, maltodextrin, acacia gum (E414), alpha-tocopherol (E307))

Lemon lime flavour (Lemon lime flavour contains: flavouring preparations, maltodextrin, mannitol (E421), gluconolactone (E575), sorbitol (E420), acacia gum (E414), colloidal anhydrous silica (E551)).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

Reconstituted solution: 24 hours

6.4 Special precautions for storage

Sachet: Do not store above 25ºC

Reconstituted solution: Store covered in a refrigerator (2ºC to 8ºC)

6.5 Nature and contents of container

The sachet is composed of paper, polyethylene/ methacrylic acid co-polymer and aluminium.

Sachets are packed in cartons of 2, 6, 8, 10, 20, 30, 50, 60 (2x30) and 100 (2x50).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

After 24 hours, any unused solution should be discarded.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 55612/0072

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/11/2013

10 DATE OF REVISION OF THE TEXT

15/01/2025